tolerance test, was observed in spite of a markedly prolonged hypoglycaemia.

COMMENT

In all five subjects studied the mean half relaxation time increased after intravenous glucose administration and decreased after intravenous insulin administration. The increase during the glucose-tolerance test was slow and lagged considerably behind the peak of blood glucose concentration, while the decrease during the insulin-tolerance test was fast and coincided with the drop in blood glucose. This difference in the time relation between blood glucose concentration and half relaxation time in the two tests makes a direct effect of blood glucose on the half relaxation time unlikely. There seems more likely to be an indirect effect, mediated perhaps through a carbohydrate-regulating hormone like adrenaline, growth hormone, or cortisol. The absence of a decrease of the half relaxation time after simultaneous administration of insulin and propranolol suggests that the changes of blood glucose influence the half relaxation time by intermediary of the adrenaline system.

Whether the changes of the Achilles tendon reflexogram in thyroid disorders and in diabetes mellitus are related to the adrenaline system requires further investigation.

SUMMARY

In five normal subjects the Achilles tendon reflex time was prolonged by intravenous glucose and shortened by intravenous insulin administration. The effect of insulin was abolished when it was given after the application of propranolol.

M. ZACHMANN, M.D.,
Paediatric Department, University of Zurich, Kinderspital, 8032 Zurich, Switzerland.

REFERENCES

Abramson, E. A., Arky, R. A., and Woeber, K. A. (1966). *Lancet*, **2**, 1386.
Beardwood, D. M., and Schumacher, L. R. (1964). *Amer. J. Med. Sci.*, **247**, 324.
Ellenberg, M. (1961). *Amer. J. med. Sci.*, **242**, 183.
Kissel, P., Debry, G., Duc, M., Vaillant, G., and Duc, M.-L. (1966). *Presse méd.*, **74**, 111.
Krosnick, A. (1964). *J. Amer. med. Ass.*, **190**, 1008.

Medical Memoranda

Foot-and-mouth Disease in Man

Brit. med. J., 1967, **4**, 529–530

Though there are numerous reports in the literature of foot-and-mouth disease in man, the total number of possible cases is still very small in relation to the frequent exposure of farmers and others to the disease in parts of the world where infection is widespread in the livestock population (Platt, 1958). In many of the reported cases the criteria on which diagnosis was based were rather less than adequate, but Pilz and Garbe (1965) described a number of cases in which the diagnosis was more completely substantiated. The virus was recovered from vesicular lesions at high titre, and significant antibody titres were developed against the strain of virus isolated from the lesions. Material from suspected cases of foot-and-mouth disease in man has been submitted to the Animal Virus Research Institute at Pirbright on several occasions, but in none of these have we been successful in isolating virus or demonstrating specific antibodies. There is, however, little doubt that the patient whose case is described below became infected with foot-and-mouth disease virus.

CASE REPORT

The patient, a man aged 35, lived on a farm with his brother, but had only indirect contact with the livestock. An outbreak of foot-and-mouth disease developed on this farm on 22 July 1966, and one of the affected animals was a cow which supplied milk used in the farmhouse. The animals were slaughtered on 24 July, and though the patient watched this operation he took no part in it.

On 28 July he complained of a slight sore throat, which became worse on the 29th. On the 30th he had a temperature of 99° F. (37.2° C.), an inflamed throat, and a few blisters on the palms and dorsa of both hands. On 31 July his temperature was normal, but the blisters on his hands had increased in number. There were two further blisters between his toes and five or six weals on the side and front of his tongue. The blisters on the backs of his hands were about 2 mm. in diameter, while those on the palmar surface were between 5 mm. and 2 cm. in diameter. The weals on the tongue were solid swellings similar in size to the blisters on the palms. There were no swellings on the fauces, soft palate, cheeks, or gums. The patient described his lesions as uncomfortable and tingling, while the tongue was hot, tingling, and sore.

Epithelium was collected from one of the blisters on the back of the hand and transferred to a container with glycerin-phosphate buffer. Two drops of fluid from another blister were added to this medium. Foot-and-mouth disease virus of type O was recovered from this material.

These lesions had regressed by 7 August, but further crops of blisters developed on the hands on 8 and 11 August and again in December. No virus was recovered from these lesions either at the Animal Virus Research Institute or at the Pathology Department of the Newcastle General Hospital. A series of blood samples were collected for antibody assay. As there was a possibility that the patient might still be a carrier of virus, throat swabs were collected at intervals and tested at both laboratories for the presence of virus. All were negative.

The patient was examined in March 1967 and again in April at the skin clinic of the Royal Victoria Hospital in Newcastle upon Tyne. The clinical syndrome was believed to be that of erythrasma and tinea pedis with a recurrent erythema multiforme. The second report stated that the hand lesions were suggestive of healing pompholyx, while some superficial erosions of the hard palate were thought to be aphthous ulcers.

LABORATORY EXAMINATION

Virus Isolation.—A suspension of epithelium collected on 31 July 1966 was inoculated into roller tube cultures of bovine thyroid cells (Snowdon, 1966). After 48 hours cytopathic change was seen and the culture fluid gave a positive reaction in the complement-fixation test with foot-and-mouth disease type O antiserum. Five days later a fresh suspension of the same epithelium was titrated in the same culture system. The epithelium was shown to contain $10^{6.4}$ TCD_{50} virus per gramme. Further epithelial samples collected on 8 and 11 August were examined, but no virus was detected. Throat swabs collected on 4 August, 21 October, and 4, 10, and 18 November also gave no evidence of virus.

Serology.—Antibody titres obtained with foot-and-mouth disease antigens are shown in the Table. Sera were collected from five veterinary officers who had been in contact with infected cattle in Northumberland and from 12 members of the staff of the Animal Virus Research Institute, all of whom had come into contact with

Antibody Titres Obtained with Foot-and-mouth Disease Antigens

Serum Samples (Days After Infection)	Neutralizing Titre. Virus Type			C.F. Titre (Overnight Fixation)
	O	A	C	
5	1/178	<1/8	<1/8	⩽16
30	1/708	<1/8	<1/8	36
40	1/355	<1/8	<1/8	54
120	1/256	<1/8	<1/8	24
154	1/80	<1/8	<1/8	Not tested

the virus of foot-and-mouth disease in the course of their normal work. All samples, tested in parallel with the serum from the patient, were negative (titre less than 1/8) except for one serum from a member of staff which showed a neutralizing titre of 1/22 against virus of type O.

Discussion

It would appear that the patient had in fact contracted an infection by the virus of foot-and-mouth disease. The lesions observed, the high titre of virus recovered from the epithelium, and the rise in antibody titre all indicate the strong probability that he became infected with foot-and-mouth disease between 24 and 31 July 1966. The high initial antibody titre was probably due to the fact that the serum was collected at least five days after the illness was first noted by the patient. The decline in antibody titre at 120 and 154 days from the beginning of the illness agrees well with the observations of Pilz and Garbe (1965).

The absence of any antibody rise in association with the recrudescence of epithelial lesions indicates that these episodes are unlikely to have anything to do with foot-and-mouth disease. But the fact that the cause of the skin condition observed in these episodes, and possibly even in the first, remains undiagnosed suggests that epithelial damage of this nature might have raised the patient's susceptibility to the foot-and-mouth disease virus. His contact with infection was less than that of many people working with infected animals in Northumberland at that time, and it is known that epithelial damage does increase the tendency to the development of lesions in experimental animals, possibly by increasing the phagocytosis of virus by epithelial cells.

The clinical signs shown in the initial illness accord with the appearance of foot-and-mouth disease in susceptible species, though the patient may also have been suffering from a skin condition of unknown origin. No spread to other humans appears to have occurred in this case, and, as the patient did not come into contact with animals either before or after his illness, there is no evidence of spread in this direction. There is, however, a clear case for restriction of movement of a suspected case in an agricultural area and for the treatment of the condition in isolation. Virus was recovered from only one of the samples—that obtained from the patient three days after the initial clinical signs. Throat swabs collected 7, 84, 98, and 106 days after infection were negative, as were epithelial samples taken at 11 and 14 days. It is therefore likely that the disease in man is relatively short-lived and that the period of infectivity is quite restricted.

R. Armstrong, M.B., B.S.,
General Practitioner, Rothbury, Northumberland.
J. Davie, B.SC., M.R.C.V.S.,
R. S. Hedger, M.R.C.V.S.,
Principal Scientific Officers, Animal Virus Research Institute, Pirbright, Surrey.

References

Pilz, W., and Garbe, H. G. (1965). *Zbl. Bact. I. Abt. Orig.*, **198**, 154.
Platt, H. (1958). *Med. Press*, **240**, 1195.
Snowdon, W. A. (1966). *Nature (Lond.)*, **210**, 1079.

Recurrent Tetanus

Brit. med. J., 1967, 4, 530

The incidence of tetanus reaches endemic proportions in Ceylon. A minimum of one case a week is admitted to any large hospital in the island. However, there is no record of a recurrence or of relapse. The following report is of a patient who had two attacks of unmistakable tetanus within three months of each other.

Case Report

An 8-year-old Sinhalese girl was admitted to hospital on 23 February 1965 with a history of difficulty in opening her mouth and repeated "convulsions" of one day's duration. She also complained of pain in the abdominal wall and severe headache. There was a history of an injury to the left lower limb, nearly a month previously, for which she was treated in the outpatient department. Immunization against tetanus had not been carried out at the time.

On examination she was found to have trismus, risus sardonicus, and rigidity of all four limbs. No spasms were observed. She was afebrile. She had been treated with pethidine 25 mg. intramuscularly on admission, and chlorpromazine 25 mg. by mouth twice a day. Crystalline penicillin 300,000 units twice daily was given by intramuscular injection. Antitetanus serum was given in an initial dose of 100,000 units intravenously, followed by 100,000 units intramuscularly. The latter was repeated daily for six days.

The patient was well enough to be discharged from hospital in 23 days from the date of admission. No active immunization had been carried out at the time. She was quite well after discharge and attended school until 30 May 1965.

On 3 June she was readmitted to hospital with trismus of four days' duration, and "convulsions" for one day. On examination she had severe trismus and a well-marked risus sardonicus. Neck stiffness was very conspicuous. No spasms were oberved. She was treated with pethidine 50 mg. and chlorpromazine 50 mg. intramuscularly six-hourly. This dosage was progressively reduced and "tailed off."

Crystalline penicillin 500,000 units intramuscularly twice daily was started, but had to be stopped on the third day, as she complained of severe itching of the body and developed an urticarial rash in both axillae. Oral tetracycline 250 mg. six-hourly was substituted. Calcium gluconate 5 ml. intravenously was given daily. An intradermal test for sensitivity to antitetanus serum was strongly positive. A weal 4.2 by 2.2 cm. developed after the diluted serum (0.1 ml.) was introduced into an area of 1 sq. cm. Thus we were unwilling to administer serum even in fractional doses. The hospital had run out of toxoid at the time, so this could not be given.

Recovery was uneventful. No spasms were noted at any time. The patient was discharged on 27 June, and was quite well except for some residual trismus. It should be noted that there was no fresh trauma to cause or provoke this second attack of tetanus.

Comment

Standard textbooks of surgery make no mention of cases of recurrent or relapsing tetanus. However, it is stated that there is no immunity conferred on a patient after an attack of tetanus. This must be so, because there are no fewer than eight antigenic strains of *Clostridium tetani* and also because neither the bacillus nor its spores are said to enter the blood stream or be carried to distant sites. Any immunity, active or passive, will be to the exotoxin, which is actively antigenic.

This case illustrates the necessity for active immunization against tetanus after an attack of the disease. This could be done with adsorbed toxoid, three 1-ml. doses at intervals of three to six weeks. A booster dose of 1 ml. of toxoid after an injury likely to produce tetanus would suffice, and is recommended.

S. Y. D. C. Wickramasinghe, M.S., F.R.C.S.,
Consultant Surgeon.
Malinie Fernando, M.B., B.S.,
House-surgeon.
General Hospital, Kandy, Ceylon.